UNIVERSITÀ
DEGLI STUDI DI MILANO-BICOCCA

COURSE SYLLABUS

Cellular Pathophysiology

2223-1-F0601Q085

Aims

The course aims to provide an interpretative framework useful to the identification of molecular targets in the diagnosis and therapy of disease. This course is ideally complementary to those on “Diseases of metabolism ” (biochemical approach) and “Gene regulation and disease” (genetic approach) in learning about disease mechanisms and therapeutic approaches.

Contents

The course will focus on themes of cellular pathophysiology with reference to different organic functions . It will deal with both gene-based abnormalities (channellopathies, signalling abnormalities.) and acquired ones (cell response to stress). To render the course suitable also for students coming from graduation courses other than Biological Sciences, the address to pathophysiology will be preceded by a succinct review of the physiological mechanisms involved..

Detailed program

The program is organized around the function of proteins with specific functions (ion channels, trasporters, etc.). The role of these proteins in different organic systems will be illustrated through examples of disease conditions (in parentesis) mechanistically linked to their abnormality. Considering the course duration (21 lessons), the program below is rather ambitious. However, every topic in the list is an independent module; therefore, it will be possible to decide during the course how many and which topics to address, depending on the students’ background knowledge and interest (new topics are introduced almost every year)

**Overview on mechanisms of transepitelial transport **

Epithelial Na+channels (ENaC)
Protein structure, function and regulation
ENaC in tubular and alveolar transport
ENaC mutations and related syndromes (pseudo-ipo & iper-aldosteronisms): epidemiology, phenotype, mechanism, therapy

Epithelial Cl-channels (CFTR, ClC, CaCC)
Protein structure, function and regulation
Cl- channels in transepitelial transport in lung, guts and glands
CFTR mutations and related syndromes (cystic fibrosis): epidemiology, multi-organ phenotype, pathogenesis , therapy

**Overview on cardiac electrophysiology and arrhythmogenic mechanisms **

V-gated Na+ channels (NaV)
Protein structure, function and regulation
NaV1.5 in cardiac excitation
Gain of function NaV1.5 mutation and the related syndrome (LQT3): epidemiology, phenotype, mechanism, therapy
Loss of function NaV1.5 mutations and related syndromes (Brugada Syndrome): epidemiology, phenotype, mechanism, therapy

V-gated and inward rectifier K+ channels
Structure, function and regulation of Kv, KCNQ, Eag, Kir proteins
Inward e delayed rectifier channels in cardiac electrophysiology and epithelial transport
Loss of function KCNQ1 mutations and the related syndrome (LQT1): epidemiology, phenotype, mechanism, therapy
Loss of function Herg mutations and the related syndrome (LQT2): epidemiology, phenotype, mechanism, therapy
Gain of function Herg mutations and the related syndrome (SQT): epidemiology, phenotype, mechanism, therapy
Loss of function Kir2.1mutations and related syndrome (Andersen-Tawil S):): epidemiology, phenotype, mechanism, therapy
Loss of function ROMK1 mutations and related syndrome (S di Bartter):): epidemiology, phenotype, mechanism, therapy

Ca2+ binding proteins and Ca2+ -dependent signaling
Calmodulins (CaM): coding, structure and function
CaMs in channel regulation (CaV1.2, RyRs, KCNQ1)
Main CaM – triggered signaling pathways: CaMK, CaN, NOS
Calmodulinopathies with LQTS phenotype:
Calmodulinopathies with CPVT phenotype

Oxygen-sensing, hypoxia and ischemia
Cellular mechanisms of oxygen sensing, oxygen-sensing organs
Hypoxia signalling
Metabolic adaptation to hypoxia
Mechanisms of cell damage in hypoxia: ROS, Ca2+ overload, mito damage
Ischemia vs hypoxia: electrical and mechanical correlates of myocardial ischemia
Post-ischemic reperfusion – mechanism of reperfusion damage
Pre- and post-conditioning in chronic ischemia

Cellular aging
Features and significance of the cellular aging process
Replicative vs stress-induced senescence: comparison of causes and mechanisms
Senescence signalling (the SASP secretosome)
Metabolic switches in senescence

Aging consequences on the cardiovascular system
Lamin mutations: The Hutchinson-Gilford Progeria syndrome

Prerequisites

Acquaintance with the contents of the courses of General and Systems Physiology (graduation course in Biological Sciences) is recommended. Depending on students' background, the teacher will decide the extent to which physiology principles shall be summarized before addressing pathophysiology; this will obviously impact on the number of topics that will be covered in the time available. Considering the impossibility to provide a single reference textbook for the course content, attendance is recommended.

Teaching form

Frontal teaching with interactive discussion. Considering the nature of the course, attendance in person is highly advised

Textbook and teaching resource

A cell Physiology textbook (e.g. Cell Physiology Sourcebook, N. Sperelakis ed., 4th edition, Academic Press) may serve as a reference for basic concepts, but it will not cover many of the specific topics presented in the course. Specific reading material, mostly in the form of review articles, will be made available during the course. Course slides will also be uploaded on the e-learning platform.
Considering the unavailability of a comprehensive textbook and the interactive teaching modality, attendance to the course is highly recommended

Semester

Second semester

Assessment method

Students will be evaluated by an oral exam. The exam, of colloquial nature, will focus on knowledge of basic mechanisms and on student's ability to apply it to the interpretation of specific conditions. Lack of acquaintance with basic principles of physics and general physiology will not be considered acceptable. Communication skills (including appropriate terminology of the discipline) will also be part of the evaluation.

Office hours

Please send email to antonio.zaza@unimib.it for appointment

Sustainable Development Goals

GOOD HEALTH AND WELL-BEING